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Authors' Affiliation:

¹Department of Gastroenterology, Dr. Sulaiman Alhabib Medical group, Arryan, Riyadh, Saudi Arabia

²Department of Cardiology, College of medicine Imam mohammad Ibn Saud Islamic university (IMSIU), Riyadh, Saudi Arabia

³Department of Rheumatology, King Saud University, Riyadh, Saudi Arabia

⁴Department of Medicine Dr. Sulaiman Alhabib Medical group, Arryan, Riyadh, Saudi Arabia

⁵Department of Pathology, King Saud University, Riyadh, Saudi Arabia

⁶Department of Histopathology and Cytology, FMLS, University of Khartoum, Sudan

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Systemic amyloidosis misdiagnosed for Crohn's disease: A case report

Salah Ahmd Elshafie¹, Khalid Alnemer², Mohammed A Omair³, Tahany Faisal Alshammari⁴, Tamam Zamil Alshammari⁵, Hussain Abdullah Aljuwayd⁴, Shayma Abduwasea Asrar⁴, Fadi Alakeel⁵, Hussain Gadelkarim Ahmed⁶

ABSTRACT

Background: Systemic amyloidosis is characterized by the steady buildup of highly structured fibrils made of autologous proteins in the organs that are affected. Our patient was often told she had Crohn's disease because she had stomach pain, diarrhea, weight loss, anemia and tiredness, but the treatment didn't work. As a result, numerous investigations and laboratory tests were performed, including gastroscopy and colonoscopy. **Conclusions:** Systemic intestinal amyloidosis can be misdiagnosed for Crohn's disease. When a similar clinical circumstance occurs, we hope that our report will remind our colleagues to be on the lookout for underlying disorders so that a quick diagnosis and successful treatment can be provided.

Keywords: Amyloidosis, Crohn's disease, abdominal pain, gastrointestinal

1. INTRODUCTION

Amyloidosis is a rare group of diseases that are caused by abnormal folding of proteins and the buildup of fibrils outside of cells. The clinical manifestation of the disease is determined by the extracellular position of these "amyloid fibril" proteins (Mann et al., 2022). These fibrils' aberrant architecture renders them intractable and difficult to eliminate, which disrupts normal tissue structure and interferes with normal functioning (Adroque, 2022).

There are 36 distinct types of amyloidosis, each of which results from a unique protein folding error. About 19 types are regarded as localized forms, 14 as systemic forms and three as those that can self-identify as either. These proteins may develop irregularities as a result of inherited environmental influences or genetic effects (Picken, 2020). Light chain (AL), inflammatory (AA), dialysis-related (A2M) and hereditary and old age (ATTR) amyloidosis are the four forms of systemic amyloidosis that occur most frequently (Ando et al., 2013).

Approximately 30 of the more than 60 identified heterogeneous amyloidogenic proteins are associated with disease in humans. All of these proteins tend to make beta-pleated sheets that are arranged in a way that is not parallel. The affected organs, including the heart, liver, kidneys, neurological system and gastrointestinal tract, experience mechanical disruption and localized oxidative stress because of these sheets' formation of inflexible, non-branching fibrils that resist proteolysis (Bhutani and Lentzsch, 2020; Baker, 2022).

The continuous deposition of autologous proteins as highly structured fibrils in target organs is what distinguishes systemic amyloidosis. The merged damage induced by the proteotoxic activity of prefibrillar species, cytotoxicity and structural abnormalities generated by amyloid fibrils, might result in organ failure that is potentially lethal. The present treatment aims to eliminate the amyloid protein and stop the amyloid cascade at its source. Amyloid fibril-specific antibodies that stimulate macrophage and giant cell phagocytosis via complement may hasten the clearance of amyloid and the recovery of organ function (Nuvolone et al., 2022).

2. THE CASES REPORT

A 34-year-old man who had recently been diagnosed with Crohn's disease was then given Azathioprine 300 mg and steroids. In November 2022, the patient was admitted to our hospital. The patient went to the emergency room (ER) with abdominal pain and diarrhea, claiming to have been hospitalized for two weeks. The characteristics of the abdominal pain were that it was all over the abdomen, was colicky in nature, was not radiated and the severity of the pain was 7/10. The abdominal pain was associated with watery diarrhea (not blooded) three times per day, which stopped two days prior to admission. The abdominal pain associated with vomiting twice per day, fatigue and exertional dyspnea and unintentional weight loss (more than 1 stone in body weight in 3 months). The patient went to the ER several times to get pain relievers and loperamide but did not improve.

Also, there are no causes that make it worse or better: No chest pain, syncope or palpitations; no fever or rashes; no discoloration of the skin; no pain or trouble swallowing; no recent travel; no history of eating outside; and no history of contact with a sick patient. There is no cough and there is no dysuria or urine frequency. There is no headache, weakness or numbness. There is no prior surgical history. There is no family history of a condition with comparable symptoms, such as a GI ailment, colorectal cancer or inflammatory bowel disease (IBD). No history of tobacco or alcohol consumption or allergies exists.

On physical examination

Vitals sign in ER BP: 107/60, T: 37, Pulse: 85, RR: 20, O₂sat: 95% on RA. Not pale or jaundiced. Mouth: No aphthous ulceration or oral thrush. Hands: No palmar erythema, Dupuytren contracture, asterixis or palpable lymph node. Abdomen: No scars or distension; caput medusa; soft, lax tenderness all over the abdomen. No palpable hepatosplenomegaly, no shifting dullness, no active bowel sounds, no bruits CNS: CGS: 15/15; cranial nerve intact; good tone; power in the upper and lower limbs 5/5; sensory and reflexes intact. CVS: S1+S2 no murmur; JVP not raised. Chest: Equal bilateral air entry; no added sounds.

Investigation

WBC: 4.45, HGB: 12.4, PLT: 227, Urea: 5.3, Creat: 98.6, K: 4.8, Na: 134, LFT: T. Bil: 16.5, D. Bil: 7.5, ALT: 9, AST: 12, AIP: 62, GGT: 16, Albumin: 27, 1.13. Corrected Ca: 2.26, Trop-I: 0.109 (0.115, 0.095), Pro-BNP: 31000>29000, Fecal Calprotectin >1000, C. diff. and stool parasitology: Negative.

ECG: low QRS voltage; ECHO: Severe congestive LVH; mild LV systolic dysfunction (EF 50% DDII); left arterial enlargement (MR RVSP 25+10).

Gastroscopy and colonoscopy

Pangastritis, duodenitis, widespread erythema, ulceration with edema at the T ileum, mucosal edema and erythema on both sides of the colon (RT>left side) were all visible. Amyloid is evidenced by the presence of numerous yellowish-white polypoid protrusions and thickening of the duodenal folds (Image 1).

Biopsy (duodenal, gastric, terminal ileum and colon): According to histopathology, the mucosa had eosinophilic amorphous material that showed apple green birefringence in polarized light of Congo red stain, which is a sign of amyloidosis (Image 2, 3).

On an MRI of the abdomen and pelvis with contrast, there was widespread thickening of the small intestine and it seemed like the colon was involved around the jejunum and distal ileum. The symptoms of Crohn's disease aren't normal, which makes it more likely that the person has a protein-losing enteropathy with fluid in the mesentery and swollen tissues under the skin.

CMR

Normal LV size and systolic function are present, as is normal wall motion. Ejection fraction ~65% with mild LVH is noted. The right ventricle is typical in size and has normal systolic function (EF > 55%) mildly dilated left atrium with an intact septum. Perfusion of the first pass of the resting myocardium is normal. As previously documented, there is a subtle heterogeneous gadolinium hyper-enhancement uptake in the myocardium normal aortic root and Valsalva sinuses and great vessels. A little pericardial effusion was discovered. T2-weighted edema imaging detects acute myocardial inflammation. Myocarditis is a possibility and the difficulties in suppressing the myocardium signal on LGE raise the possibility of amyloidosis.



Image 1 (A) Amyloid is marked by multiple yellowish-white polypoid growths and thickening of the folds in the lower part of the duodenum

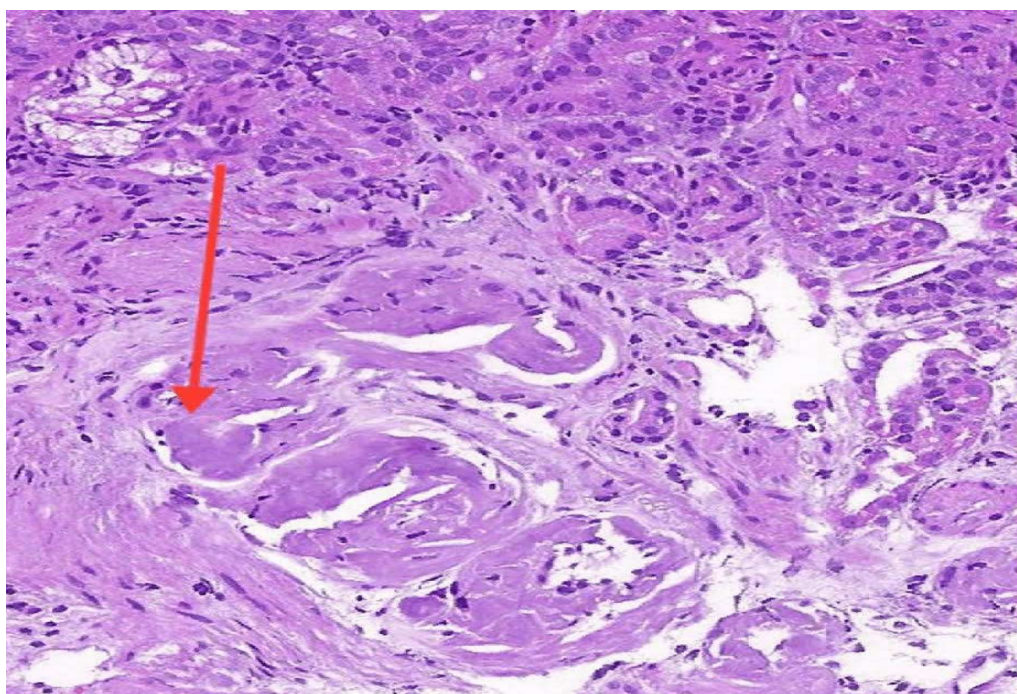


Image 2 With amyloidosis, there is amorphous, eosinophilic material in the mucosa that looks apple green under polarized light

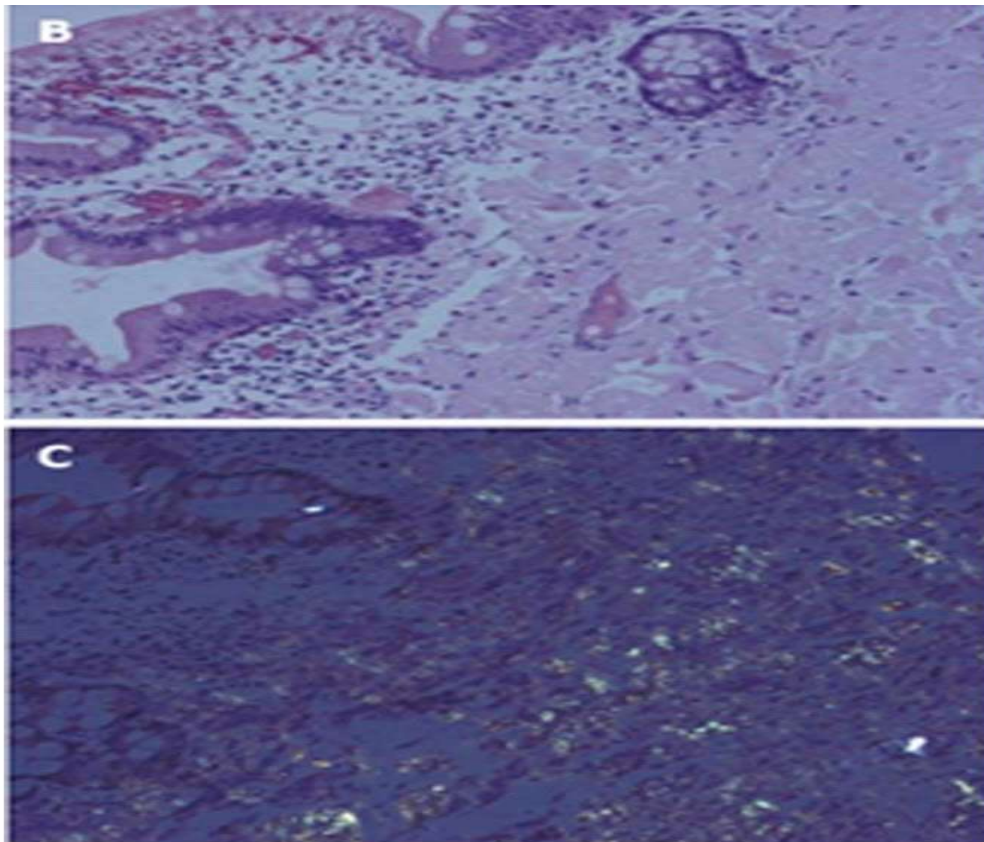


Image 3 (B): Histopathology sections revealed significant homogeneous eosinophilic accumulation in the mucosae and submucosa; (C): Under polarized light, Congo red stain confirmed a peculiar "apple-green" birefringence of amyloid formation

3. DISCUSSION

Crohn's disease (CD), an autoimmune disease that affects the whole gastrointestinal tract, is a subtype of IBD. CD-induced bowel injury and disability are a major global health concern. Genetic vulnerability and environmental variables such as a westernized lifestyle are all well-known risk factors for CD (Cheng et al., 2021). CD is thought to be a complex ailment with a diverse etiology in which genetics and environment interact to cause the disease. Several genes have been examined in relation to CD; however, the strongest and most replicated connections have been found with the NOD2, IL23R and ATG16L1 genes (Gajendran et al., 2018). The presence of extra-intestinal signs, the degree of involvement, the severity of the disease and the progression of complications can all affect the associated symptoms. Numerous conditions can mimic Crohn's disease, creating difficulties in diagnosis. They include gastrointestinal luminal tract illnesses, vascular disease, autoimmune diseases, infections, malignancies and their consequences, drug or medical procedure-induced ailments and hereditary diseases. To make the right diagnosis, potential reasons must be carefully taken into account (Gupta and Allegratti, 2022).

Secondary amyloidosis is a serious but rare complication of IBD. It most often happens in people with Crohn's disease. Amyloidosis affects at least 1% of Crohn's disease patients. According to the research that has been conducted, the time that passes between the onset of Crohn's disease and the identification of amyloidosis can range anywhere from one to twenty-one years (Basturk et al., 2009). The prevalence of amyloidosis among individuals with IBD is 0.53% (95% confidence interval (CI): 0.32-0.75), despite epidemiological evidence showing that it may be under diagnosed. Males with aggressive and severe Crohn's disease are the phenotype most usually linked to amyloidosis (Tosca-Cuquerella et al., 2016). With a prevalence of 1%, Crohn's disease (CD) is the IBD condition most frequently associated with AA amyloidosis, meaning that 1 in every 95 CD patients may have systemic amyloidosis (Barahona-Correa et al., 2021).

4. CONCLUSION

Systemic intestinal amyloidosis can be misdiagnosed for Crohn's disease. When a similar clinical circumstance occurs, we hope that our report will remind our colleagues to be on the lookout for underlying disorders so that a quick diagnosis and successful treatment can be provided.

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Author Contributions

Salah Ahmd Elshafie: Conception, case analysis, manuscript drafting, approval of the final version.

Khalid Alnemer: Case analysis, manuscript drafting, approval of the final version.

Mohammed A Omair, Tahany Faisal Alshammari and Tamam Zamil Alshammari: Case analysis, manuscript drafting, approval of the final version.

Hussain Abdullah Aljuwayd and Shayma Abduwasea Asrar: Case analysis, manuscript drafting, approval of the final version.

Fadi Alakeel: Case analysis, manuscript drafting, approval of the final version.

Hussain Gadelkarim Ahmed: Supervision, critical revision of manuscript, approval of the final version.

Informed consent

Written & Oral informed consent was obtained from the patient.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

REFERENCES AND NOTES

- Adroque HE. Amyloidosis of the Heart and Kidney. *Methodist Debaque Cardiovasc J* 2022; 18(4):27-33. doi: 10.14797/mdcvj.1150
- Ando Y, Coelho T, Berk JL, Cruz MW, Ericzon BG, Ikeda S, Lewis WD, Obici L, Planté-Bordeneuve V, Rapezzi C, Said G, Salvi F. Guideline of transthyretin-related hereditary amyloidosis for clinicians. *Orphanet J Rare Dis* 2013; 8:31. doi: 10.1186/1750-1172-8-31
- Baker KR. Light Chain Amyloidosis: Epidemiology, Staging and Prognostication. *Methodist Debaque Cardiovasc J* 2022; 18(2):27-35. doi: 10.14797/mdcvj.1070
- Barahona-Correa JE, Morales SD, Andrade-Pérez R, Hani A. Renal Amyloidosis and Crohn Disease. *Ochsner J* 2021; 21(3):291-295. doi: 10.31486/toj.20.0129
- Basturk T, Ozagari A, Ozturk T, Kusaslan R, Unsal A. Crohn's disease and secondary amyloidosis: Early complication? A case report and review of the literature. *J Ren Care* 2009; 35(3):147-50. doi: 10.1111/j.1755-6686.2009.00106.x
- Bhutani D, Lentzsch S. Diagnosis and management of systemic light chain AL amyloidosis. *Pharmacol Ther* 2020; 214:107612. doi: 10.1016/j.pharmthera.2020.107612
- Cheng WX, Ren Y, Lu MM, Xu LL, Gao JG, Chen D, Kalyani FS, Lv ZY, Chen CX, Ji F, Lin HN, Jin X. Palmitoylation in Crohn's disease: Current status and future directions. *World J Gastroenterol* 2021; 27(48):8201-8215. doi: 10.3748/wjg.v27.i48.8201
- Gajendran M, Loganathan P, Catinella AP, Hashash JG. A comprehensive review and update on Crohn's disease. *Dis Mon* 2018; 64(2):20-57. doi: 10.1016/j.disamonth.2017.07.001
- Gupta S, Allegretti JR. Mimics of Crohn's Disease. *Gastroenterol Clin North Am* 2022; 51(2):241-269. doi: 10.1016/j.gtc.2021.12.006
- Mann BK, Bhandohal JS, Cobos E, Chitturi C, Eppanapally S. LECT-2 amyloidosis: What do we know? *J Investig Med* 2022; 70(2):348-353. doi: 10.1136/jim-2021-002149
- Nuvolone M, Nevone A, Merlini G. Targeting Amyloid Fibrils by Passive Immunotherapy in Systemic Amyloidosis. *BioDrugs* 2022; 36(5):591-608. doi: 10.1007/s40259-022-00550-w
- Picken MM. The Pathology of Amyloidosis in Classification: A Review. *Acta Haematol* 2020; 143(4):322-334. doi: 10.1159/000506696
- Tosca-Cuquerella J, Bosca-Watts MM, Anton-Ausejo R, Tejedor-Alonso S, De-Miguel FM, Minguez-Perez M. Amyloidosis in Inflammatory Bowel Disease: A Systematic Review of Epidemiology, Clinical Features and Treatment. *J Crohns Colitis* 2016; 10(10):1245-53. doi: 10.1093/ecco-jcc/jjw080